# EXHIBIT 4

U.S. Department of Health and Human Services

# MEDWATCH

**The FDA Safety Information and Adverse Event Reporting Program**

For use by user-facilities, distributors and manufacturers for MANDATORY reporting



Approved by FDA on 10/25/2002

Mfr report # NSADSS2002025716

UF/Dist report #

FDA use only

## A. Patient information

| 1. Patient identifier | 2. Age at time of event: or Date of birth: | 3. Sex | 4. Weight |
|---|---|---|---|
| DMN<br>In confidence | 31 Year<br>04/12/1970 | [ ] female<br>[X] male | 203 lbs<br>or<br>_____ kgs |

## B. Adverse event or product problem

1. [X] Adverse event and/or [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse (check all that apply)
- [X] death 05/29/2003 (mo/day/yr)
- [X] life-threatening
- [X] hospitalization - initial or prolonged
- [X] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [X] other: Med Signif

| 3. Date of event (mo/day/yr) | 4. Date of this report (mo/day/yr) |
|---|---|
| 05/12/2002 | |

5. Describe event or problem

TREAT Registry:

A 31 year-old man who initiated infliximab (dose unknown) on 17-Apr-99 to treat Crohn's disease enrolled in the TREAT Registry on 09-Dec-99. It is unclear if the patient received 1 or 2 infliximab infusions prior to baseline. No infliximab infusions subsequent to enrollment were reported. The patient received mercaptopurine, mesalamine, methotrexate, prednisone, narcotic analgesics and other Crohn's therapy (NOS) in the year prior to TREAT registration. The patient was diagnosed with T-delta gamma lymphoma. He had experienced symptom onset in early May-02. The patient received

(Cont.)

6. Relevant test/laboratory data, including dates

No Relevant Test/Laboratory Data Reported

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

(Cont.)

## C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1 REMICADE (INFLIXIMAB, RECOMBINANT) Lyophilized Powder
#2 6-MP (MERCAPTOPURINE)

| 2. Dose, frequency & route used | 3. Therapy dates (from/to (or best estimate)) |
|---|---|
| #1 (Cont.) | #1 04/17/1999-04/17/1999 |
| #2 | #2 ??/??/????-05/12/2002 |

| 4. Diagnosis for use (indication) | 5. Event abated after use stopped or dose reduced | 6. Lot # (if known) | 7. Exp. date (if known) | 8. Event reappeared after reintroduction |
|---|---|---|---|---|
| #1 CROHN'S DISEASE | #1 [ ] yes [ ] no [X] doesn't apply | #1 | #1 | #1 [ ] yes [ ] no [X] doesn't apply |
| #2 CROHN'S DISEASE | #2 [ ] yes [ ] no [ ] doesn't apply UNK | #2 | #2 | #2 [ ] yes [ ] no [ ] doesn't apply UNK |

9. NDC # -for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)

No Concomitant Products Reported

## G. All manufacturers

1. Contact office - name/address (& mfring site for devices)

2. Phone number

3. Report source (check all that apply)
- [ ] foreign
- [X] study
- [ ] literature
- [ ] consumer
- [X] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (mo/day/yr)
08/06/2003

5. (A)NDA # _____
IND # _____
PLA # 98-0012
pre - 1938 [ ] yes
OTC product [ ] yes

6. If IND, protocol #
TREAT REGISTRY

7. Type of report (check all that apply)
- [ ] 5-day
- [ ] 15-day
- [ ] 10-day
- [ ] periodic
- [ ] initial
- [ ] follow-up # ___

8. Adverse event term(s)
1)NON-HODGKIN'S LYMPHOMA

9. Mfr. report number
NSADSS2002025716

## E. Initial reporter

1. Name & address
Anonymous/Refused
UNITED STATES

phone #

| 2. Health professional? | 3. Occupation | 4. Initial reporter also sent report to FDA |
|---|---|---|
| [X] yes [ ] no | Physician | [ ] yes [ ] no [X] unk |

FDA 3500A Facsimile

**Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.**

Approved by FDA on 10/25/2002

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**The FDA Safety Information and Adverse Event Reporting Program**

For use by user-facilities, distributors and manufacturers for MANDATORY reporting



Mfr report # NSADSS2002025716

UF/Dist report #

FDA use only

## A. Patient information

1. Patient identifier — In confidence

2. Age at time of event: or Date of birth:

3. Sex: ☐ female ☐ male

4. Weight: _____ lbs or _____ kgs

## B. Adverse event or product problem

1. ☐ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse (check all that apply)
- ☐ death _____ (mo/day/yr)
- ☐ life-threatening
- ☐ hospitalization - initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other: _____

3. Date of event (mo/day/yr)

4. Date of this report (mo/day/yr)

5. Describe event or problem

6. Relevant test/laboratory data, including dates

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

## C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#3 MESALAMINE (MESALAZINE)
#4

2. Dose, frequency & route used
#3
#4

3. Therapy dates from/to (or best estimate)
#3 ??/??/????-??/??/????
#4

4. Diagnosis for use (indication)
#3 CROHN'S DISEASE
#4

5. Event abated after use stopped or dose reduced
#3 ☐ yes ☐ no ☐ doesn't apply
UNK
#4 ☐ yes ☐ no ☐ doesn't apply

6. Lot # (if known)
#3
#4

7. Exp. date (if known)
#3
#4

8. Event reappeared after reintroduction
#3 ☐ yes ☐ no ☐ doesn't apply
UNK
#4 ☐ yes ☐ no ☐ doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)

## G. All manufactures

1. Contact office - name/address (& mfring site for devices)

2. Phone number

3. Report source (check all that apply)
- ☐ foreign
- ☐ study
- ☐ literature
- ☐ consumer
- ☐ health professional
- ☐ user facility
- ☐ company representive
- ☐ distributor
- ☐ other: _____

4. Date received by manufacturer (mo/day/yr)

5. (A)NDA # _____
IND # _____
PLA # _____
pre - 1938 ☐ yes
OTC product ☐ yes

6. If IND, protcol #

7. Type of report (check all that apply)
- ☐ 5-day ☐ 15-day
- ☐ 10-day ☐ periodic
- ☐ initial ☐ follow-up # ____

8. Adverse event term(s)

9. Mfr. report number

## E. Initial reporter

1. Name & address

phone #

2. Health professional? ☐ yes ☐ no

3. Occupation

4. Initial reporter also sent report to FDA ☐ yes ☐ no ☐ unk

FDA 3500A Facsimile

**Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.**

Mfr. report#: NSADSS2002025716

Continuation Sheet for FDA-3500A Form | Page 3 of 3 | Date of this report :

**B5. Describe event or problem (Cont...)**

unspecified treatment, and the event was not resolved. Concomitant medication at the time of the event included mercaptopurine and mesalamine. The event was reported to be life threatening, required hospitalization and caused persistent disability or incapacity. The event was considered to be possibly related to current drug treatment for Crohn's disease and not related to Crohn's disease.

Additional information received 06-AUG-2003:

Medical history was updated. The event onset date was corrected to 12-MAY-2002. Mercaptopurine was discontinued on 12-MAY-2002. The patient was reported to have died due to T delta gamma lymphoma on 20-MAY-2003. It is unknown if an autopsy was performed. Reporter causality remains unchanged.

**B.7 Other relevant history, including preexisting medical conditions (Cont...)**

**Other relevant medical history**

Crohn's disease diagnosed 1999 (colon only). Treated with mercaptopurine, mesalamine, methotrexate, prednisone, narcotic analgesics and other Crohn's therapy (NOS) in the year prior to TREAT registration (09-Dec-99).

Other Med. Rel Info:Med Signif

Additional information received 06-AUG-2003:

Previously treated with antibiotics, steroids.

**C. Suspect medication (Cont...)**

| | |
|---|---|
| **Seq No.** | : 1 |
| **C.1 Suspect medication** | : REMICADE (INFLIXIMAB, RECOMBINANT) Lyophilized Powder |
| **C.2 dose,frequency & route used** | : 1) , 1 in 1 Day, Intravenous Drip |